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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 09/721,904 | 11/27/2000 | Michael H. Julius | 47841/00063 | 4246 |
| 27871 | 7590 | 11/18/2003 | EXAMINER | |
| BLAKE, CASSELS & GRAYDON LLP BOX 25, COMMERCE COURT WEST 199 BAY STREET, SUITE 2800 TORONTO, ON M5L 1A9 CANADA | | | TELLER, ROY R | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1654 | |

DATE MAILED: 11/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/721,904

Applicant(s)

JULIUS ET AL.

Examiner

Roy Teller

Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 159,161-163,170-178,180-191,193-195,198-202 and 222-255 is/are pending in the application.
- 4a) Of the above claim(s) 177,178,181-186,190,191 and 195 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 159,161-163,170-178,180-191,193-195,198-202 and 222-255 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3-20, 3-21 6) ☐ Other: _____

DETAILED ACTION

This office action is in response to the amendment, received 9/8/03, in which applicant amended claims 159, 161-163, 188-189, and 200-201; cancelled claims 160, 164-169, 179, 192, 196-198, and 203-221; and added new claims 228-255. Claims 177, 178, 181-186, 190-191, and 195 have been withdrawn.

Claims 159, 161-163, 170-176, 180, 187-189, 193, 194, 198-202, and 222-255 are pending and will be examined as they read on the elected species of HNP1 and SEQ ID NO: 4.

Information Disclosure Statement

The information disclosures statements, received 3/20/03 and 3/21/03, are acknowledged. A signed copy of each is included hereto.

Claim Rejections - 35 USC § 102

Claims 163, 170-176, 180, 199-202, 222-223, and 226-227 stand rejected under 35 U.S.C. 102 (c) as being anticipated by Julius (USPN 6,093,693) for the reasons of record.

Applicant's arguments were carefully considered but were not found persuasive.

Applicant contends that Julius teaches activation of B cells by CD14. Applicant states that there is no suggestion that exposure of epithelial cells will result in the production of a defensin.

The applied reference has a common SEQ ID NO:4 with the instant application. Julius teaches a method of activating B cells in a mammal, by administering CD14, see abstract. Julius discloses SEQ ID NO: 4 which is a 100% query match with SEQ ID NO:4 of the instant application, see STIC search. Julius teaches that CD14 can be administered to an infant, by incorporating CD14 into infant formula, see abstract. Julius discloses CD14 protein purified from bovine colostrum whey, see abstract. Julius teaches administration could be by any convenient means, see column 18, line 8.

Claim Rejections - 35 USC § 103

Claims 159, 161-163, 187-189, 193-194, 198, and 224-225 stand rejected under 35 U.S.C. 103(a) as being anticipated by Diamond (Proc. Natl. Acad. Sci., vol. 93, pp 5156-5160, May 1996) in view of Julius (USPN 6,093,693) for the reasons of record.

Applicant's arguments were carefully considered but were not found persuasive

Applicant contends that the invention defined by the claims require stimulating or enhancing expression of at least one defensin by directly exposing epithelial cells or epidermis to soluble CD14 (or equivalent), is neither taught, nor suggested by the teachings of Diamond, alone or in combination with Julius.

The claimed invention is drawn to a method of stimulating expression of defensin by administering a compound comprising soluble CD14 to epithelial cells of a mammal. The protein has an amino acid sequence of at least about 63%, 68%, 71%, 73%, 78% 83%, 88%, 93%, or 98% conserved in relation to SEQ ID NO:4.

Diamond teaches tracheal epithelial cells exposed to bacterial lipopolysaccharides express CD14, see abstract. Diamond discloses a widespread mechanism of host defense in the animal kingdom is the production of antibiotic peptides/ defensins, see page 5156, column 1, paragraph 2. Diamond teaches the soluble form of CD14 can mediate lipopolysaccharide-stimulated responses in epithelial cells, see page 5157, column 2, paragraph 4. Diamond discloses *in vivo* evidence for increased expression of B-defensin lingual antibiotic peptide in the squamous epithelium of the tongue, see page 5159, column 2, paragraph 2. Diamond does not teach a structure of CD14.

Julius teaches a method of activating B cells in a mammal, by administering CD14, see abstract. Julius discloses SEQ ID NO: 4 which is a 100% query match with SEQ ID NO:4 of the instant application, see STIC search. Julius teaches that CD14 can be administered to an infant, by incorporating CD14 into infant formula, see abstract. Julius discloses CD14 protein purified from bovine colostrum whey, see abstract.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have added the teachings of Diamond to protein of Julius in order to enhance expression of antibiotic peptides/ defensins because Diamond teaches that many mammalian epithelial cells have the capacity for analogous host defense responses.

New Rejections

Claim Rejections - 35 USC § 102

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 228-255 are rejected under 35 U.S.C. 102(e) as being anticipated by Julius (USPN 6,093,693).

The applied reference has a common SEQ ID NO:4 with the instant application. Julius teaches a method of activating B cells in a mammal, by administering CD14, see abstract. Julius discloses SEQ ID NO: 4 which is a 100% query match with SEQ ID NO:4 of the instant application, see STIC search. Julius teaches that CD14 can be administered to an infant, by incorporating CD14 into infant formula, see abstract. Julius discloses CD14 protein purified from bovine colostrum whey, see abstract. Julius teaches administration could be by any convenient means, see column 18, line 8.

Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 228-255 are rejected under 35 U.S.C. 103(a) as being unpatentable over Diamond (Proc. Natl. Acad. Sci., vol. 93, pp 5156-5160, May 1996) in view of Julius (USPN 6,093,693).

The claimed invention is drawn to a method of stimulating expression of defensin by administering a compound comprising soluble CD14 to epithelial cells of a mammal. The protein has an amino acid sequence of at least about 63%, 68%, 71%, 73%, 78%, 83%, 88%, 93%, or 98% conserved in relation to SEQ ID NO:4.

Diamond teaches tracheal epithelial cells exposed to bacterial lipopolysaccharides express CD14, see abstract. Diamond discloses a widespread mechanism of host defense in the animal kingdom is the production of antibiotic peptides/ defensins, see page 5156, column 1, paragraph 2. Diamond teaches the soluble form of CD14 can mediate lipopolysaccharide-stimulated responses in epithelial cells, see page 5157, column 2, paragraph 4. Diamond discloses *in vivo* evidence for increased expression of *B*-defensin lingual antibiotic peptide in the squamous epithelium of the tongue, see page 5159, column 2, paragraph 2. Diamond does not teach a structure of CD14.

Julius teaches a method of activating B cells in a mammal, by administering CD14, see abstract. Julius discloses SEQ ID NO: 4 which is a 100% query match with SEQ ID NO:4 of the instant application, see STIC search. Julius teaches that CD14 can be administered to an infant, by incorporating CD14 into infant formula, see abstract. Julius discloses CD14 protein purified from bovine colostrum whey, see abstract.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have added the teachings of Diamond to protein of Julius in order to enhance expression of antibiotic peptides/ defensins because Diamond teaches that many mammalian epithelial cells have the capacity for analogous host defense responses.

Conclusion

All claims are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roy Teller whose telephone number is (703)305-4243. The examiner can normally be reached on Monday-Friday from 5:30 am to 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (703) 306-3220. The fax phone number for the organization where this application or proceeding is assigned is (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

RT
1654
11/14/03

RT



CHRISTOPHER R. TATE
PRIMARY EXAMINER